

## REMARKS

Favorable reconsideration is earnestly solicited.

Claims 3-8, 10, 12, 15-17, 35-47, 55 and 57-63 are pending. Non-elected claims 5-8, 10, 12, 15-16, 35-47 and 55 were withdrawn from consideration by the Examiner. Claims 3-4, 17 and 57-63 are being examined and were rejected in the Office Action dated July 26, 2006. Rejoinder of claims 5-8 is requested upon allowance of claims 3-4.

### *35 U.S.C. 112 – Definiteness*

Claims 3-4, 17 and 57-63 were rejected under Section 112, second paragraph, as being allegedly “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants traverse.

The term “complex” is replaced with the term “conjugate” to more clearly define technical features of the invention, as suggested by the Examiner. It is believed that the rejection is rendered moot by the amendment.

Therefore, withdrawal of the rejection is requested.

### *35 U.S.C. 112 – Enablement*

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 3-4, 17, 57 and 63 were rejected under Section 112, first paragraph, because it was alleged that the specification does not reasonably provide enablement for isolated conjugates comprising derivatives of ubiquitin with fragments and derivatives of proteins formed via the N-end rule mechanism. Applicants traverse.

The Examiner based his rejection on the alleged unpredictability in the art with regard to the tertiary structure required for the interaction of substrate with the cognate E3 ubiquitin-protein ligase enzymes.

But a person skilled in the art would be able to practice the subject invention without undue experimentation in view of the disclosure in the specification and further in view of the high level of skill in the relevant art.

The “enablement” prong of the first paragraph of 35 U.S.C. 112 requires nothing more than objective enablement. Whether this is achieved by illustrative examples or by broad terminology is of no importance. *In re Marzocchi*, 169 USPQ 367 (CCPA 1971). Enablement is not precluded by the necessity for some experimentation such as routine screening, but the experimentation needed to practice the invention must not be undue experimentation. The key word is undue, not experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, (Fed. Cir. 1988).

Applicants urge that the experimentation required to practice the full scope of the pending claims is reasonable and not undue, as a skilled artisan regularly engages in such experimentation.

The specification enables a skilled artisan to create fragments of proteins of the disclosed sequence and to conduct in vitro N-end rule pathway ubiquitylation screening, as described in the specification, to determine which fragments are ubiquitylated via N-end rule pathway. The specification also enables a skilled artisan to synthesize protein fragments, to derivatize them, and to determine which fragments are subject to N-end rule ubiquitylation by conducting in vitro N-end rule pathway ubiquitylation screening, as described in the specification.

The specification provides guidance to a skilled artisan by defining the claimed fragments and derivatives (specification at page 43, lines 9-22), and by providing numerous examples of ubiquitylated protein fragments of the claimed proteins characterized by gel electrophoresis (see specification at pages 41-42 providing molecular weight and cleavage position estimates for characterized protein fragments, Examples 2-6, and corresponding gel electrophoresis images in Figures 3-7).

The in vitro N-end rule ubiquitylation screen disclosed in the specification allows a skilled artisan to rapidly evaluate all selected fragments and derivatives: “The activity of these proteins as ubiquitylation substrates can be determined by measuring the accumulation of ubiquitylated products” (specification at page 40, lines 11-13, and working examples on pages 76-89).

Such experimentation is not undue. A person skilled in the art would, therefore, have a significant amount of confidence and information available to guide them in selecting and predicting the activity of ubiquitin fragments and derivatives.

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) and M.P.E.P. § 2164.06,

The test for enablement is whether one reasonably skilled in the art to make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. A patent may be enabling even though some experimentation is necessary. *United States v. Telectronics, Inc.*) 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988).

Applicants urge that any experimentation that may be required would be routine in the art. Therefore, the pending claims are enabled by the disclosure in the specification and withdrawal of the rejection is requested.

#### *Conclusions and Request for Interview*

In view of the above, Applicants submit that the claims are in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Moreover, due to the highly technical nature of issues which were present in responding to this Office Action, Applicants believe that an interview would be helpful in addressing any issues which were not successfully traversed in this response or over-


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come by this response. Thus, Applicants respectfully request an interview with the Examiner after this response has been reviewed.

Respectfully submitted,

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